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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,426	09/30/2003	Jen-Wei Chiao	15741.003	2704

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,426	CHIAO ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/30/03 and 12/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received July 16, 2007.

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Agnieszka Boesen Art Unit 1648.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/30/2003 and 12/10/2003 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 11-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite, "A method of activating or augmenting an immune system (...), which method comprises administering an isothiocyanate (ITC) based agent to a mammal in need of such treatment (...)." It is not clear if the recitation of the phrase "a mammal in need of <u>such</u> treatment" refers to a mammal in need of activating the immune system or a mammal in need of administering the ITC. Clarification and correction is required.

Claim 21 recites, "(...) wherein the antigen is associated with a xenogeneic cell or antigen." It is not clear what is the type of "association" between the antigen and the xenogeneic cell. Additionally, it is not clear what type of antigen Applicants consider as the "xenogeneic antign". The specification does not define the claimed "association" or the "xenogeneic antigen". Correction and clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 7, 10-13, and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the claimed methods in the BALB/c nude mice, does not reasonably provide enablement for practicing the claimed methods in patient populations having AIDS, SARS, an immunodeficiency, an infection, or a condition relating to insufficient T-cell function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to methods of activating or augmenting an immune system of a patient having an immunodeficiency, an infection, a condition relating to insufficient T-cell function and a patient that has AIDS or SARS, the method comprising administering an isothiocyanate (ITC) based agent, wherein the ITC-based agent is PEITC-NAC or PEITC.

The claims are rejected because the specification does not provide sufficient enablement to practice the claimed method in the patient populations having AIDS, SARS, an

immunodeficiency, an infection, or a condition relating to insufficient T-cell function. Additionally, the specification does not provide sufficient enablement to practice the claimed method, wherein the PEITC-NAC or PEITC is administered in combination with a vaccine.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors deemed relevant are those of the amount of direction and the working examples provided, that quantity of experimentation necessary, the (un)predictability of the art, and the breadth of the claims.

The specification provides working examples showing an increase in the number of B and NK cells in tissue surrounding tumor and in peripheral blood of PEITC-NAC fed mice xenografted with human prostate cancer PC-3 cells, as compared to the control mice that did not receive the PEITC-NAC diet. The specification does not provide working examples evidencing that administration of PEITC-NAC or PEITC in a patient having an infection, an immunodeficiency or a patient having AIDS or SARS can result in activation of the immune system. The specification does not provide working examples evidencing that PEITC-NAC or

PEITC administered in combination with a vaccine has an adjuvant effect to augment an immune response.

Based on the experimental results obtained from the nude BALB/c mouse model, the skilled artisan would be unable to reasonably conclude that the administration of PEITC-NAC or PEITC in the claimed patient populations will result in activating the particular components of the immune system. The skilled artisan would expect that the immune responses to PEITC-NAC or PEITC would be different in each and every patient population. Particularly, the immune responses will differ in the immuno-compromised patient population that is in patients having an immunodeficiency or AIDS, versus patient populations with a normal immune system but infected with SARS or other pathogens. The mice used in the working examples of the specification are nude BALB/c mice that lack thymus and therefore have a small population of T cells and a low response to T-cell dependent antigens. The antibody response in those mice is confined to IgM class and these mice are characterized by a compensatory increase in the level of NK cells resulting in an increase of the level of NK cells in comparison to normal, not-nude BALB/c mice (see the phenotype information, Taconic, pages 1-5). The present claims broadly refer to an immunodeficiency, while there are a number of known immunodeficiencies affecting different components of the immune system. The skilled artisan would expect that depending on a type of an immunodeficiency, in some cases the PEITC-NAC or PEITC could activate an immune system, while in other cases particularly in patients affected with SCID (severe combined immune deficiency) or in patients with NK cell defect, the administration of PEITC-NAC or PEITC would not increase the production antigen-specific antibodies or activate the NK cell system, as required by the claims. Similarly, in patients diagnosed with AIDS, who lack

functional T-helper cells, which are required for the generation of the antigen-specific antibodies from plasma cells, it is unlikely that the administration of PEITC-NAC or PEITC will activate the production of antigen-specific antibodies.

Thus without undue experimentation, the skilled artisan would be unable to conclude that administration of PEITC-NAC or PEITC in patients with an immunodeficiency or patients diagnosed with AIDS, would result in activation of an immune system. Without an undue experimentation testing the effects of PEITC-NAC or PEITC in patients having SARS or any other infection, the skilled artisan would be unable to conclude, based on the examples in the present specification, that administration of PEITC-NAC or PEITC to the said patient populations will have the claimed effects.

To the contrary of the present disclosure, the art teaches hat PEITC-NAC and PEITC have rather inhibitory effect on the immune system. Dey et al. (The Journal of Pharmacology and Experimental Therapeutics, 2006, Vol. 317, p. 326-333) teach an anti-inflammatory activity of PEITC-NAC and PEITC through interference with transcription of proinflammatory genes.

There is absence of a teaching in the art about activating an immune system by administration of PEITC-NAC or PEITC in patient populations having AIDS, SARS, an immunodeficiency, an infection, or a condition relating to insufficient T-cell function. The *in vitro* studies elucidating the mechanism of action of PEITC-NAC and PEITC indicate that PEITC-NAC and PEITC exert their effect by activating and stimulating macrophages and cyclin-dependent kinase inhibitors (see Xu et al. Biochemical Pharmacology, 2000, Vol. 60, p. 221-231) and Chen et al. Planta Medica, 2003, Vol. 69, p. 696-700).

Applicants have not provided convincing evidence that administration of PEITC-NAC and/or PEITC can result in activation of an immune system in patient populations affected with an immunodeficiency, an infection, or in patients that have AIDS or SARS. One would require conducting an undue amount of experimentation in order to positively conclude that administration of PEITC-NAC or PEITC would result in activation of the specific components of the immune system as required by the claims. The specification does not provide sufficient guidance to practice the claimed methods with a reasonable expectation of success and thus in the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 1, 3, 4, 6, 8, 13, 14, 16, 19, 20, and 23-25 under 35 U.S.C. 102(b) as being anticipated by Sherr et al. (US 6,407,062 B1) **is withdrawn** in view of Applicant's arguments.

Rejection of claims 1, 6-8, 10-14, 16, 19, and 21-22 under 35 U.S.C. 102(b) as being anticipated by Moore et al. (US 2002/0164694 A1) **is withdrawn** in view of Applicant's arguments.

New Rejection

Claims 1-5, 8, 9, 14-19, 21, 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Chung et al. (US Patent 6,433,011 B1) as evidenced by Xu et al. (Biochemical Pharmacology, 2000, Vol. 60, p. 221-231) and Chen et al. (Planta Medica, 2003, Vol. 69, p. 696-700).

Claims are drawn to a method of activating or augmenting an immune system of a mammal to increase the production of antigen-specific antibodies or innate immunity response to antigen, comprising administering an isothiocyanate (ITC) based agent, wherein the ITC-based agent is PEITC-NAC or PEITC. The mammal is a patient having cancer. The ITC based agent is administered orally, intravenously or topically.

Chung discloses a method of inhibiting formation of colon cancer in a mammal, comprising administering to the mammal a pharmacologically effective amount of PEITC or PEITC-NAC (see claims 1-12, and column 2, lines 44-65). Because Chung is administering the same compounds PEITC or PEITC-NAC to a mammal, as the compounds being administered in the present method, Chung's compounds have the same properties as the compounds of the present invention. Therefore Chung's PEITC and PEITC-NAC posses the properties and functions recited in the present claims and thus Chung anticipates the present methods of activating an immune system, wherein the PEITC or PEITC-NAC activate the production of specific antibodies in response to antigen, activate the NK cell system to destroy cancer cells, increase the levels of cyclin-dependent kinase inhibitors, reduce expression of cyclin D and E, and inhibit Rb phosphorylation in cancers cells.

The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property, which is inherently present in the prior art, does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

It is understood that the function of the PEITC and PEITC-NAC remains the same regardless of the source of antigen (cancer antigen or xenogeneic antigen). Thus the recitation of the source of antigen as being associated with the xenogeneic cell is not limiting. It is also noted that the claims do not recite the administration of PEITC or PEITC-NAC in combination with an antigen.

Chung discloses oral administration of PEITC or PEITC-NAC (see column 3, line 66 to column 4 lines 1-3 and column 6, lines 43-46).

The references by Chen and Xu are cited for evidence purposes showing that the mechanism of action of PEITC and PEITC-NAC, such as activation of an immune system (see Chen et al) and increase of the levels of the cyclin-dependent kinase inhibitors (see Xu et al), were known in the art at the time the present invention was made.

Thus Chung anticipates the present claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of claims 2, 15, 17, and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062 B1) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above and in view of Ghai et al. (US 5,955,269) **is withdrawn** in view of Applicant's arguments.

Rejection of claim 2, 15, 17, and 20 under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (US 2002/0164694 A1) as applied to claims 1, 6-8, 10-14, 16, 19, and 21-22 above and in view of Ghai et al. (US 5,955,269) **is withdrawn** in view of Applicant's arguments.

Rejection of claim 5, 9, and 18 under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062 B1) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above and in view of Horan et al. (US 5,665,328) **is withdrawn** in view of Applicant's arguments.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AB

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